Applicant: Susan Lindquist Attorney's Docket No.: 17481-004001 / WI WHI03-

23/UC UCHI:702/MIT10247W

Serial No.: 09/207,649

Filed: December 8, 1998

Page : 2 of 9

## Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

## **Listing of Claims**:

- 1. (Currently Amended) A method of identifying a candidate substance that inhibits the aggregation of a mammalian aggregate-prone amyloid protein <u>in a yeast cell</u>, comprising:
- (a) contacting a yeast cell that expresses a chimeric aggregate-prone amyloid protein comprising a mammalian aggregate-prone amyloid peptide with said candidate substance under conditions effective to allow aggregated amyloid formation in the yeast cell; and
- (b) determining the ability of said candidate substance to inhibit the aggregation of the aggregate-prone amyloid protein in the yeast cell.

## 2. (Cancelled)

3. (Previously Presented) The method of claim 1, wherein the mammalian aggregate-prone amyloid protein comprises a PrP or  $\beta$ -amyloid polypeptide.

## 4-6. (Cancelled)

- 7. (Previously Presented) The method of claim 1, wherein the chimeric protein comprises at least an aggregate forming domain of a mammalian aggregate-prone amyloid protein operably attached to a detectable marker protein.
- 8. (Original) The method of claim 7, wherein said marker protein is green fluorescent protein or luciferase.

Attorney's Docket No.: 17481-004001 / WI WHI03-Applicant: Susan Lindquist 23/UC UCHI:702/MIT10247W

Serial No.: 09/207,649

: December 8, 1998 Filed

Page : 3 of 9

9. (Original) The method of claim 7, wherein said marker protein is a drug-resistance marker protein.

- 10. (Original) The method of claim 7, wherein said marker protein is a hormone receptor.
- 11. (Original) The method of claim 10, wherein said hormone receptor is a glucocorticoid receptor.
- 12. (Previously Presented) The method of claim 1, wherein the chimeric protein comprises at least an aggregate forming domain of PrP or  $\beta$ -amyloid.
- 13. (Original) The method of claim 12, wherein the chimeric protein comprises at least about amino acids 1-42 of β-amyloid protein.
- 14. (Previously Presented) The method of claim 1, wherein the chimeric protein comprises Sup35 in which the N-terminal domain has been replaced by amino acids 1-42 of βamyloid protein.
- 15. (Previously Presented) The method of claim 1, wherein any aggregation of the mammalian aggregate-prone amyloid protein is detected by the ability of the aggregated protein to bind Congo Red.
- 16. (Previously Presented) The method of claim 1, wherein any aggregation of the mammalian aggregate-prone amyloid protein is detected by increased protease resistance of the aggregated protein.
- 17. (Original) The method of claim 1, wherein the aggregate-prone amyloid protein is labeled.

Applicant: Susan Lindquist Attorney's Docket No.: 17481-004001 / WI WHI03-Serial No.: 09/207,649 23/UC UCHI:702/MIT10247W

Filed: December 8, 1998

Page : 4 of 9

, 0 .

18. (Original) The method of claim 17, wherein the label is a radioactive isotope, a fluorophore, or a chromophore.

- 19. (Original) The method of claim 18, wherein the label is <sup>35</sup>S.
- 20. (Original) The method of claim 18, wherein the fluorophore comprises a green fluorescent protein polypeptide.
  - 21. (Cancelled)
  - 22. (Original) The method of claim 1, wherein said yeast cell overexpresses Hsp104.
  - 23-36. (Cancelled)
- 37. (Previously Presented) The method of claim 1, wherein aggregated amyloid formation is evidenced by the formation of fibrillary material.
  - 38-40. (Cancelled)